AUGUST 2009

Dear Healthcare Professional:

In June 2009, Genzyme Corporation issued a press release announcing the detection of a virus in its recombinant cell cultures that produce the enzyme replacement therapy (ERT), imiglucerase. The contamination of cell cultures resulted in the immediate interruption of drug production and the subsequent supply shortage of Cerezyme® (imiglucerase) for some patients for a period of time. Since the announcement, Actelion has received direct requests from Healthcare Professionals for information regarding Zavesca® (miglustat) as an immediate option for patients who may not have access to imiglucerase treatment during the shortage.

Actelion would like to inform physicians that Zavesca® is indicated for the treatment of adult patients with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (e.g. due to constraints such as allergy, hypersensitivity or poor venous access). Zavesca® was approved and has been marketed in the United States since 2003. The decision to prescribe Zavesca® to patients is at the discretion of the treating physician. The physician should assess the risks and benefits of therapy for the individual patient.

Clinical studies where patients were switched from Cerezyme® to Zavesca® monotherapy have been conducted. One of these studies is described as follows:

- The Study OGT 918-004 was a prospective, open-label, randomized clinical study over 24 months in which type 1 Gaucher patients were switched from ERT to Zavesca® monotherapy in one treatment arm. There were no significant differences for mean absolute changes in liver, spleen volume and hemoglobin concentration between the groups of patients switched to Zavesca® monotherapy and the Cerezyme® group. However, in adult type 1 Gaucher disease patients who had been treated with enzyme replacement therapy for at least 2 years, switching to Zavesca® as monotherapy was associated with decreases in platelet counts after discontinuation of enzyme replacement therapy. Platelet counts also declined after discontinuation of enzyme replacement therapy in patients originally randomized to combination therapy. [USPI; Elstein et al, Blood, 2007, 110(7):2296-2301]

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Important Safety Information for Zavesca®

- Gastrointestinal disturbances (GI) such as diarrhea, flatulence and abdominal pain are the most common adverse side reactions associated with Zavesca® therapy.
  - Diarrhea due to Zavesca® therapy usually responds to the introduction of a lactose-free and low carbohydrate diet and/or loperamide treatment.
- Peripheral neuropathy has been reported in patients receiving Zavesca®.
  - Patients should undergo neurological examination at the start of treatment and every 6 months thereafter; Zavesca® should be reassessed in patients who develop symptoms of peripheral neuropathy.
- Zavesca® may cause fetal harm if administered to a pregnant woman.
  - Pregnancy category X; Zavesca® is contraindicated in women who are or who may become pregnant; patients should be appraised of the potential hazard to a fetus.
- There is a risk of impaired fertility in men.
  - Men should maintain reliable contraceptive methods and not plan to conceive while taking Zavesca® and for 3 months after discontinuing treatment.
- There is no experience with the use of Zavesca® in type 1 Gaucher disease patients under the age of 18 years.

Please consult the enclosed Zavesca® package insert for complete prescribing information. If you have additional questions or require additional information, please contact the Medical Information Department at **usmedinfo@actelion.com** or call toll-free (866) 228-3546 and follow the prompts for Medical Information.

Sincerely,

Kirk Taylor, MD
Senior Vice President, US Medical

Stefan Kolb, MD
Global Medical Leader, Zavesca®

Enclosure: Zavesca USPI 2008

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